REMARKS/ARGUMENTS

I. Status of the Claims

Claims 1-35 and 42-47 were pending for purposes of this Office Action, as claims 40 and 41 were previously cancelled by way of preliminary amendment dated October 6, 2005 and claims 36 to 39 were previously cancelled in response to a Restriction Requirement.

Claim 1 has been amended without prejudice to incorporate features of claims 3, 11, 19 and 20. Claims 3, 11, 19 and 20 have been cancelled without prejudice by way of the present amendment. Claims 4, 12, 21, 22, 24 and 27 have been amended to establish proper antecedent basis since claims 3, 11, 19 and 20 have been cancelled without prejudice by way of the present amendment.

Claims 1, 2, 4 to 10, 12 to 18, 21 to 35 and 42 to 47 remain pending.

Reconsideration is respectfully requested.

II. Double Patenting

In the Office Action, claims 1-2, 11-14, 19, 22-23 and 27 to 37 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4 of copending U.S. Application No. 10/413, 022.

In the Office Action, claims 1-2, 10-18 and 23 to 26 were also provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 to 11, 16 and 30 to 33of copending U.S. Application No. 10/621, 964.

In response, Applicants respectfully submit that the filing of a terminal disclaimer will be considered upon notification that the pending claims are otherwise allowable.

III. Claim Rejections- 35 U.S.C. § 102

In the current Office Action, claims 1, 2, 4, 5, 7 to 11, 15 to 19, 24, 26, 27 and 42 were rejected under 35 U.S.C. § 102(b) as being anticipated by Gupta et al. (U.S. 2002/0006933).

The Gupta publication, US 2002/0006933, is concerned with treating sexual dysfunction using apomorphine.

Independent claim 1 of the present invention, as amended, recites: "A composition for treating sexual dysfunction by pulmonary inhalation, said composition comprising apomorphine, the apomorphine being in the form of a free base, pharmaceutically acceptable salt or ester, wherein the composition provides a nominal dose of apomorphine of from about 100 to about 1600 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt); wherein the administration of the composition by pulmonary inhalation provides a Cmax within 1 to 5 minutes of administration; wherein the composition is a dry powder composition; and wherein the apomorphine has a mass median aerodynamic diameter of 10 μm or less."

The Gupta reference does not show or teach a composition that "provides a nominal dose of apomorphine of from about 100 to about 1600 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt); wherein the administration of the composition by pulmonary inhalation provides a Cmax within 1 to 5 minutes of administration" as recited in amended claim 1 of the present invention.

The present Response refers primarily to independent claim 1 of the present invention, however, the patentability of the dependent claims 2, 4, 5, 7 to 10, 15 to 18, 24, 26, 27 and 42 follow at least for the reason of being dependent, either directly or indirectly, from the independent claim 1 that is patentable. Claims 11 and 19 have been cancelled without prejudice, therefore, the rejection under 35 U.S.C. § 102(b) of claims 11 and 19 are moot.

In view of the foregoing, reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) to claims 1, 2, 4, 5, 7 to 11, 15 to 19, 24, 26, 27 and 42 as being anticipated by Gupta et al. (U.S. 2002/0006933) is respectfully requested.

IV. Claim Rejections- 35 U.S.C. § 103

Gupta et al. in view of Lucas et al.:

In the current Office Action, claims 3, 6, 12 to 14, 20 to 23, 25, and 28 were rejected under 35 U.S.C. 103(a) as being unpatentable over Gupta et al. (U.S. Publication No. 2002/0006933) as applied to Claims 1 to 2, 4 to 5, 7 to 11, 15 to 19, 24, 26 to 27, and 42 in view of Lucas et al. (Pharmaceutical Research 1999, Vol. 16, No. 10, pgs. 1643-1647).

Independent claim 1 as amended recites: "A composition for treating sexual dysfunction by pulmonary inhalation, said composition comprising apomorphine, the apomorphine being in the form of a free base, pharmaceutically acceptable salt or ester, wherein the composition provides a nominal dose of apomorphine of from about 100 to about 1600 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt); wherein the administration of the composition by pulmonary inhalation provides a Cmax within 1 to 5 minutes of administration; wherein the composition is a dry powder composition; and wherein the apomorphine has a mass median aerodynamic diameter of 10 μm or less."

The claims of the present invention are directed to a composition for treating sexual dysfunction by pulmonary inhalation of a dry powder composition comprising a low dose of apomorphine (100-1600 μg), wherein the administration of the composition by pulmonary inhalation provides a Cmax within 1 to 5 minutes of administration.

The Gupta publication, US 2002/0006933, is concerned with treating sexual dysfunction using apomorphine. However, the Gupta reference does not teach or suggest "a nominal dose of apomorphine of from about 100 to about 1600 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt)" as recited in claim 1 of the present invention. The Examiner's attention is directed to paragraph [0074] of the Gupta publication, where it is stated that "[a]n 8 mg human dose compares well with about 1.33 mg apomorphine dose in dogs." Applicants submit that the inhaled dose range described in the Gupta publication US2002/0006933 is equivalent to a 3-12 mg human dose

range – well above the 0.1-1.6 mg dose as claimed for the subject invention. Thus, the Gupta reference does not teach or suggest "a nominal dose of apomorphine of from about 100 to about 1600 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt)" as recited in claim 1 of the present invention.

The Gupta reference also does not teach or suggest a composition "wherein the administration of the composition by pulmonary inhalation provides a Cmax within 1 to 5 minutes of administration" as recited in amended claim 1 of the present invention. Applicants respectfully submit that given the nature of the disorder being treated by the present invention, ie sexual dysfunction including erectile dysfunction, the speed of therapeutic response is a very important parameter in effective therapy. The ability to achieve a very rapid C max (Cmax within 1 to 5 minutes of administration) as recited in claim 1 of the present invention is unpredictable and unexpected. None of the prior art references cited by the Examiner discloses such a rapid Tmax (recited in amended claim 1 as "Cmax within 1 to 5 minutes of administration") as currently claimed. Indeed, the fastest Tmax seen in Gupta in dogs is 0 .17 hours, for inhalation and "inhalation" (more specifically, instillation, as described below). This equates to 10.2 minutes. In contrast, in the present invention, the Tmax is achieved within 1 to 5 minutes of administration, more than twice as fast, and up to 10 times as fast using inhaled apomorphine having a particle size of 10 microns or less. This result is supported by the human clinical trial data provided in Figure 16 of the present application which show a Tmax of ~ 1 minute. Thus the Gupta reference does not teach or suggest the unexpected result of the present invention of the ability of the composition to achieve a very rapid C max ("Cmax within 1 to 5 minutes of administration") as recited in claim 1 of the present invention. None of the prior art references cited by the Examiner discloses such a rapid Cmax (recited in amended claim 1 as "Cmax within 1 to 5 minutes of administration") as currently claimed.

The Gupta publication, as shown in Example 2 of Gupta, discloses the administration of apomorphine by instillation (i.e., using a solution), as a *model* of inhalation. Applicants respectfully submit that instillation is not always good model for inhalation and does not allow predictions to be made about inhalation. Applicant's following submissions substantiate the point that instillation is an unsuitable model of inhalation. Thus, certain limitations are inherent

in the teaching provided by the Gupta publication, and would not have made obvious the specific invention as now claimed in the subject application. In fact, Gupta does not disclose inhalation in any form, but only describes instillation as a model of inhalation. Instillation is the use of a solution to deliver a drug, to represent administration of an aerosolized drug. Applicants attach herewith as Appendix A, a paper entitled "Pulmonary Distribution of Particles Given by Intratracheal Instillation or by Aerosol Inhalation" which discloses that the distribution pattern of intratracheally instilled particles differs considerably from that produced following inhalation of comparable particles. See Brain *et al.,* "Pulmonary Distribution of Particles Given by Intratracheal Instillation or by Aerosol Inhalation," Environmental Research, volume 11, pages 13-33, 1976. Pathological studies demonstrate that instillation results in heavy more centralized deposits, whereas the inhalation pattern is lighter and both, more evenly and more widely distributed. See Brain *et al.,* "Pulmonary Distribution of Particles Given by Intratracheal Instillation or by Aerosol Inhalation," Environmental Research, volume 11, conclusion section. Accordingly, it is not possible to draw conclusions regarding the inevitable effects of inhalation of a component from an instillation experiment of the same component. However, even if instillation is considered by the Examiner to be a suitable model for inhalation, then the "inhalation" Tmax of Gupta is 0 .17 hours in dogs. Therefore, achieving a Cmax within 1 to 5 minutes of administration in humans (Tmax of a maximum of five minutes (0.083 hours)) as recited in claim 1, is twice as fast as in Gupta, and was not predictable from the teaching in dogs of Gupta.

In addition, Applicants assert that while pharmacokinetic parameters were presented in Example 2 of the Gupta publication, there were no pharmacodynamic data presented or even commented upon. Accordingly, there is nothing in the Gupta publication (which describes only the use of apomorphine solution, and only speculates that powder compositions can be used) that teaches or suggests that inhalation of apomorphine powder, at the doses tested, could achieve a therapeutic effect. In addition, where Gupta does refer to pharmacokinetic parameters in humans, in table 7, the fastest Tmax achieved is 0.34 hours using a subcutaneous approach. Although Table 7 of Gupta only discloses data for sublingual and subcutaneous Tmax values, Applicants note that in both cases the Tmax is slower in humans than it is for the equivalent delivery route in dogs. Therefore, Applicants respectfully submit that the same may then be

expected for the inhalation route as well. In complete contrast, using the present formulation and dose, the present invention achieves a quicker Tmax. Accordingly, it is completely unexpected that using the composition of the present invention for pulmonary inhalation, a Tmax of 1 to 5 minutes can be achieved.

Furthermore, the apomorphine solution of Gupta does not have to undergo dissolution of the drug because it is already in a form suitable for transport across the lung. The powdered formulation of the present invention is particulate apomorphine. When administered to the lung the particulate apomorphine must undergo dissolution in the lung fluid before transport/permeation across the lung epithelium. The dissolution of the particles takes additional time but still achieves a faster Tmax than a liquid administration. Thus, the rapid response observed with the dry powder inhalation is yet more surprising. As noted above, the Gupta reference does not teach or suggest the unexpected result of the present invention of the ability of the composition to achieve a very rapid C max ("Cmax within 1 to 5 minutes of administration") as recited in claim 1 of the present invention. None of the prior art references cited by the Examiner discloses such a rapid Cmax (recited in amended claim 1 as "Cmax within 1 to 5 minutes of administration") as currently claimed.

Certainly, the Gupta publication does not teach or suggest a powder composition "wherein the administration of the composition by pulmonary inhalation provides a Cmax within 1 to 5 minutes of administration" as recited in amended claim 1 of the present invention. As noted above, Applicants respectfully submit that Gupta does not teach inhalation in any way, but merely teaches installation as a model for inhalation. Data for instillation is described in Table 4 of the Gupta publication. As shown in Table 4 of the Gupta publication, the doses of apomorphine administered by "inhalation" (using instillation as a model) led to a C_{max} being achieved after 0.17 h, which is more than 10 minutes after administration. The rapid uptake of apomorphine into the blood following inhalation of the powdered formulations of the present invention means that C_{max} is reached quickly. Thus, Applicants believe the Gupta publication does not meet the limitations of low dose, rapid effect, and lack of associated side effects as recited for the claimed invention. Moreover, Applicants believe there is no teaching or suggestion in US2002/0006933 that would lead a person of ordinary skill in the art to modify

what is described in the Gupta publication and thereby arrive at the claimed dose, time to therapeutic effect, and lack of associated side effects, as claimed.

Applicants respectfully submit that it is inappropriate for the Examiner not to consider the teaching of Gupta as a whole, but rather to focus only on the instillation/inhalation portion of the description. Applicants remind the Examiner that a prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. See W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984). Applicants respectfully submit that a person of ordinary skill in the art reading Gupta as a whole would not be motivated to develop a human dosage form for apomorphine delivery through inhalation, on the logical assumption that it would invariably be accompanied by immediate emesis. When considering Gupta as a whole, it is apparent that other routes of delivery given in Gupta appear to be preferable to instillation. It is noted that the Gupta publication shows the inhalation route of administration, itself, is a contributory factor in the incidence of emesis observed. For example, in Gupta, the inhalation of a dose of 1 mg apomorphine led to a C_{max} of 31.5 ng/ml (Table 4). The administration of 20 mg apomorphine by oral gavage led to a very similar C_{max} of 29.3 ng/ml (Table 6). However, all five dogs in the instillation/inhalation study suffered immediate emesis upon inhaling the dose of apomorphine (Table 3). In contrast, only two out of five dogs suffered immediate emesis following the oral dose of apomorphine (Table 5). Table 2 of the Gupta reference, intranasal delivery of apomorphine gives a C_{max} in the range of 139 and 1,152 ng per ml. This is much higher than via the instillation route given in Table 4, where C_{max} ranges from 15 to 65. The skilled person would, therefore, consider intranasal administration to be more preferable route of administration for apomorphine than instillation. As shown in Table 3 of Gupta, the incidence of emesis in dogs is 100% for the instillation model for apomorphine administration. In comparison, the emesis effect is far less severe for other delivery routes, such as intranasal or oral delivery. Accordingly, given the teaching of Gupta, a skilled person would prefer other approaches, such as intranasal or oral delivery over instillation/inhalation. The skilled person certainly would not have expected the benefits that are associated with the inhalation of powder formulations of the present invention, namely the rapid onset of a therapeutic effect, using a

relatively low dose, yet without induction of the adverse side effects normally associated with the administration of apomorphine.

Lucas et al., (Pharmaceutical Research, 1999; 16(10):1643-1647) does not cure aforementioned defects of the Gupta publication. Specifically, Lucas et al. fails to teach a composition that "provides a nominal dose of apomorphine of from about 100 to about 1600 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt)" as recited in amended claim 1 of the present invention. In fact, while Lucas et al. is concerned with inhalation therapy, and is cited for describing similar particle size ranges or excipients/propellants used for an inhalation composition, Lucas et al. does not relate to apomorphine or treatments for sexual dysfunction and thus cannot be readily adapted to, or readily applied to modify, the teaching of the Gupta publication in order to cure the defects of the primary reference.

Lucas et al. does not describe a composition "wherein the administration of the composition by pulmonary inhalation provides a Cmax within 1 to 5 minutes of administration" as recited in amended claim 1 of the present invention. A person skilled in the art concerned with the administration of apomorphine for the treatment of sexual dysfunction would therefore not find in the Lucas reference any teaching or suggestion regarding the relatively low dose and relatively rapid onset of therapeutic effect provided by the subject invention, which are claimed in the subject application, but are clearly missing from the Gupta publication.

Therefore, inhalation of a "composition comprising apomorphine, the apomorphine being in the form of a free base, pharmaceutically acceptable salt or ester, wherein the composition provides a nominal dose of apomorphine of from about 100 to about 1600 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt); wherein the administration of the composition by pulmonary inhalation provides a Cmax within 1 to 5 minutes of administration" as recited in amended claim 1 of the present invention would not have been obvious from the Gupta publication, taken alone, or in combination with the Lucas et al. reference.

The present Response refers primarily to independent claim 1 of the present invention, however, the patentability of the dependent claims 2 to 28 and 42 follow at least for the reason of being dependent from the independent claim 1 that is patentable. Claims 3, 11, 19 and 20 have been cancelled without prejudice, therefore, the rejection under 35 U.S.C. § 103(a) of claims 3, 11, 19 and 20 are moot.

In view of the foregoing, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) to claims 1 to 28 and 42 as being unpatentable over Gupta et al. (U.S. 2002/0006933) in view of Lucas et al. (Pharmaceutical Research 1999, Vol. 16, No. 10, pgs. 1643-1647) is respectfully requested.

Gupta et al. in view of Vervaet et al.:

In the current Office Action, claims 29 to 35 were rejected under 35 U.S.C. 103(a) as being unpatentable over Gupta et al. (U.S. Publication No. 2002/0006933) as applied to Claims 1 to 2, 4 to 5, 7 to 11, 15 to 19, 24, 26 to 27, and 42 above and in further view of Vervaet et al. (International Journal of Pharmaceutics, 1999, Vol. 186, pgs. 13-30).

The Gupta reference is discussed above with respect to independent claim 1 of the present invention. Claims 29 to 35 depend, either directly or indirectly from claim1

Vervaet et al. describes "an overview of the present state of the art with respect to the formulation of MDIs." See Vervaet, abstract.

Vervaet et al. (International Journal of Pharmaceutics, 1999, Vol. 186, pgs. 13-30) does not cure aforementioned defects of the Gupta publication. Specifically, Vervaet et al. fails to teach a composition that "provides a nominal dose of apomorphine of from about 100 to about 1600 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt)" as recited in amended claim 1 of the present invention. Vervaet et al. does not relate to apomorphine or treatments for sexual dysfunction and thus cannot be readily adapted to, or readily applied to modify, the teaching of the Gupta publication in order to cure the defects of the primary reference.

Vervaet et al. does not describe a composition "wherein the administration of the composition by pulmonary inhalation provides a Cmax within 1 to 5 minutes of administration" as recited in amended claim 1 of the present invention. A person skilled in the art concerned with the administration of apomorphine for the treatment of sexual dysfunction would therefore not find in the Vervaet et al. reference any teaching or suggestion regarding the relatively low dose and relatively rapid onset of therapeutic effect provided by the subject invention, which are claimed in the subject application, but are clearly missing from the Gupta publication.

Therefore, inhalation of a "composition comprising apomorphine, the apomorphine being in the form of a free base, pharmaceutically acceptable salt or ester, wherein the composition provides a nominal dose of apomorphine of from about 100 to about 1600 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt); wherein the administration of the composition by pulmonary inhalation provides a Cmax within 1 to 5 minutes of administration" as recited in amended claim 1 of the present invention would not have been obvious from the Gupta publication, taken alone, or in combination with the Vervaet et al. reference.

As discussed above, the present Response refers primarily to independent claim 1 of the present invention, however, the patentability of the dependent claims 29 to 35 follow at least for the reason of being dependent from the independent claim 1 that is patentable.

In view of the foregoing, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) to claims 29 to 35 as being unpatentable over Gupta et al. (U.S. 2002/0006933) in view of Vervaet et al. (International Journal of Pharmaceutics, 1999, Vol. 186, pgs. 13-30) is respectfully requested.

Gupta et al. in view of Pierre et al.:

In the current Office Action, claims 43 to 44 were rejected under 35 U.S.C. 103(a) as being unpatentable over Gupta et al. (U.S. Publication No. 2002/0006933) as applied to Claims 1 to 2, 4 to 5, 7 to 11, 15 to 19, 24, 26 to 27, and 42 above and in further view of Pierre et al.

(Annals of Allergy, Asthma and Immunology, April 1999, Vol. 82, No. 4, pgs. 377-382, abstract).

The Gupta reference is discussed above with respect to independent claim 1 of the present invention. Claims 43 and 44 depend indirectly from claim 1.

Pierre et al. describes a study which "compares the efficacy and safety of one and two actuations of albuterol sulfate powder delivered via a breath-actuated, effort-assisted, investigational inhaler (Spiros, Dura Pharmaceuticals, Inc) and albuterol delivered via a conventional propellant-driven metered dose inhaler (Ventolin, Glaxo, Inc)." See Pierre et al., abstract.

Pierre et al. does not cure aforementioned defects of the Gupta publication. Specifically, Pierre et al. fails to teach a composition that "provides a nominal dose of apomorphine of from about 100 to about 1600 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt)" as recited in amended claim 1 of the present invention. Pierre et al. does not relate to apomorphine or treatments for sexual dysfunction and thus cannot be readily adapted to, or readily applied to modify, the teaching of the Gupta publication in order to cure the defects of the primary reference.

Pierre et al. does not describe an apomorphine composition "wherein the administration of the composition by pulmonary inhalation provides a Cmax within 1 to 5 minutes of administration" as recited in amended claim 1 of the present invention. A person skilled in the art concerned with the administration of apomorphine for the treatment of sexual dysfunction would therefore not find in the Pierre et al. reference any teaching or suggestion regarding the relatively low dose and relatively rapid onset of therapeutic effect provided by the subject invention, which are claimed in the subject application, but are clearly missing from the Gupta publication.

Therefore, inhalation of a "composition comprising apomorphine, the apomorphine being in the form of a free base, pharmaceutically acceptable salt or ester, wherein the composition

provides a nominal dose of apomorphine of from about 100 to about 1600 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt); wherein the administration of the composition by pulmonary inhalation provides a Cmax within 1 to 5 minutes of administration" as recited in amended claim 1 of the present invention would not have been obvious from the Gupta publication, taken alone, or in combination with the Pierre et al. reference.

As discussed above, the present Response refers primarily to independent claim 1 of the present invention, however, the patentability of the dependent claims 43 and 44 follow at least for the reason of being dependent from the independent claim 1 that is patentable.

In view of the foregoing, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) to claims 43 and 44 as being unpatentable over Gupta et al. (U.S. 2002/0006933) in view of Pierre et al. (Annals of Allergy, Asthma and Immunology, April 1999, Vol. 82, No. 4, pgs. 377-382, abstract) is respectfully requested.

Gupta et al. in view of Snow et al.:

In the current Office Action, claims 45 to 47 were rejected under 35 U.S.C. 103(a) as being unpatentable over Gupta et al. (U.S. Publication No. 2002/0006933) as applied to Claims 1 to 2, 4 to 5, 7 to 11, 15 to 19, 24, 26 to 27, and 42 above and in further view of Snow (U.S. Publication No. 2002/0134382).

The Gupta reference is discussed above with respect to independent claim 1 of the present invention. Claims 45 to 47 depend indirectly from claim1.

Snow (U.S. Publication No. 2002/0134382) describes "a medicament container configured to improve entrainment of the medicament in the air and to improve deposition of the medicament in the lungs includes an upper layer and a bottom layer with medicament disposed therebetween." See Snow, abstract.

The Snow publication does not cure aforementioned defects of the Gupta publication. Specifically, the Snow publication fails to teach a composition that "provides a nominal dose of apomorphine of from about 100 to about 1600 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt)" as recited in amended claim 1 of the present invention. The Snow publication does not relate to apomorphine or treatments for sexual dysfunction and thus cannot be readily adapted to, or readily applied to modify, the teaching of the Gupta publication in order to cure the defects of the primary reference.

The Snow publication does not describe an apomorphine composition "wherein the administration of the composition by pulmonary inhalation provides a Cmax within 1 to 5 minutes of administration" as recited in amended claim 1 of the present invention. A person skilled in the art concerned with the administration of apomorphine for the treatment of sexual dysfunction would therefore not find in the Snow publication any teaching or suggestion regarding the relatively low dose and relatively rapid onset of therapeutic effect provided by the subject invention, which are claimed in the subject application, but are clearly missing from the Gupta publication.

Therefore, inhalation of a "composition comprising apomorphine, the apomorphine being in the form of a free base, pharmaceutically acceptable salt or ester, wherein the composition provides a nominal dose of apomorphine of from about 100 to about 1600 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt); wherein the administration of the composition by pulmonary inhalation provides a Cmax within 1 to 5 minutes of administration" as recited in amended claim 1 of the present invention would not have been obvious from the Gupta publication, taken alone, or in combination with the Snow publication.

As discussed above, the present Response refers primarily to independent claim 1 of the present invention, however, the patentability of the dependent claims 45 to 47 follow at least for the reason of being indirectly dependent from the independent claim 1 that is patentable.

In view of the foregoing, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) to claims 45 to 47 as being unpatentable over Gupta et al. (U.S. 2002/0006933) in view of Snow (U.S. Publication No. 2002/0134382) is respectfully requested.

CONCLUSION

Reconsideration of the present application, as amended, is requested. The Examiner is respectfully requested to telephone Applicant's undersigned attorney in order to resolve any outstanding issues and advance the prosecution of the case to allowance.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,
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